

## AMENDMENTS

### Amendments to the Claims:

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Claim 1 (currently amended): A chemically defined valency platform molecule comprising ~~at least one~~ a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Daltons.

Claims 2-16 (withdrawn)

Claim 17 (original): A conjugate of a valency platform molecule of claim 1 and a biologically active molecule.

a'  
Claim 18 (currently amended): The conjugate of claim 17, wherein the biologically active molecule is selected from the group consisting of ~~poly(saccharides), poly(amino acids), nucleic acids and lipids~~ a polysaccharide, a polypeptide, a nucleic acid, and a lipid.

Claim 19 (original): The conjugate of claim 17, wherein the conjugate is a B cell toleragen.

Claim 20 (withdrawn)

Claim 21 (currently amended): The conjugate of claim 19, wherein the biologically active molecule is a  $\beta_2$ GPI domain 1 polypeptide or analog thereof that specifically binds to a  $\beta_2$ GPI-dependent antiphospholipid antibody.

Claim 22 (original): The conjugate of claim 21, wherein the conjugate is effective for the treatment of antibody mediated thrombosis.

Claim 23 (original): The conjugate of claim 18, wherein the biologically active molecule is an  $\alpha$ Gal epitope or analog thereof that specifically binds to an anti- $\alpha$ Gal antibody.

Claim 24 (original): A pharmaceutically acceptable composition comprising the conjugate of claim 17 and a pharmaceutically acceptable carrier.

a<sup>1</sup>  
Claim 25 (currently amended): A conjugate of a chemically defined valency platform molecule and a polypeptide comprising a  $\beta_2$ GPI domain 1 polypeptide, wherein the conjugate comprises ~~at least one~~ a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Daltons.

Claim 26 (original): The conjugate of claim 25, wherein the valency platform molecule comprises at least 3 aminooxy groups.

Claim 27 (original): The conjugate of claim 25, wherein the valency platform molecule comprises at least 3 carbamate groups.

Claim 28 (currently amended): The conjugate of claim 25, wherein the high molecular weight polyethylene oxide group has a molecular weight greater than about 22,000 Daltons.

Claim 29 (original): The conjugate of claim 25, wherein the valency platform molecule comprises a core group and at least three arms, wherein each arm comprises a terminus.

Claim 30 (original): The conjugate of claim 25, wherein the polypeptide specifically binds to a  $\beta_2$ GPI-dependent antiphospholipid antibody.

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Claim 31 (original): The conjugate of claim 30, wherein the polypeptide lacks a T cell epitope capable of activating T cells in an individual having  $\beta_2$ GPI dependent antiphospholipid antibodies.

Claim 32 (original): The conjugate of claim 25, wherein the  $\beta_2$ GPI domain 1 polypeptide comprises at least five contiguous amino acids of Figure 19 (SEQ ID NO: 2).

Claim 33 (original): The conjugate of claim 25, wherein the  $\beta_2$ GPI domain 1 polypeptide comprises amino acids Nos. 2-63 of SEQ ID NO: 2.

Claim 34 (currently amended): The conjugate of claim 25, wherein the conjugate is selected from the group consisting of compounds 200, 202, 203, and 205 shown in Figure 7 and

compound 300 shown in Figure 16, wherein D1 in said structures is a polypeptide consisting of amino acids No. 2-63 of SEQ ID No: NO: 2.

Claim 35 (new): The conjugate of claim 23, wherein the biologically active molecule is an  $\alpha$ Gal epitope.

Claim 36 (new): The conjugate of claim 25, wherein the conjugate is effective for the treatment of antibody mediated thrombosis.

Claim 37 (new): The conjugate of claim 17, wherein the total molecular weight of the conjugate is no greater than about 200,000 Daltons.

a  
Claim 38 (new): The conjugate of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 22,000 Daltons.

Claim 39 (new): The conjugate of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 30,000 Daltons.

Claim 40 (new): The conjugate of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 40,000 Daltons.

Claim 41 (new): The conjugate of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 50,000 Daltons.

Claim 42 (new): The conjugate of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 100,000 Daltons.

Claim 43 (new): The conjugate of claim 17, wherein the high molecular weight polyethylene oxide group has the formula:



wherein n is greater than about 500.

Claim 44 (new): The conjugate of claim 43, wherein n is greater than about 600.

Claim 45 (new): The conjugate of claim 43, wherein n is greater than about 700.

a<sup>1</sup>  
Claim 46 (new): The conjugate of claim 43, wherein n is greater than about 800.

Claim 47 (new): The conjugate of claim 43, wherein n is greater than about 900.

Claim 48 (new): The conjugate of claim 43, wherein n is about 400 to 550.

Claim 49 (new): The conjugate of claim 43, wherein n is 520 to 600.

Claim 50 (new): The conjugate of claim 43, wherein n is 600 to 800.

Claim 51 (new): The conjugate of claim 43, wherein n is 600 to 1000.

Claim 52 (new): The conjugate of claim 17, wherein the valency platform molecule comprises a second high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.

Claim 53 (new): The conjugate of claim 17, wherein the valency platform molecule comprises a core group and at least three arms wherein each arm comprises a terminus.

Claim 54 (new): The conjugate of claim 53, wherein the core group comprises the high molecular weight polyethylene oxide group.

a<sup>1</sup> Claim 55 (new): The conjugate of claim 53, wherein one of said arms comprises the high molecular weight polyethylene oxide group.

Claim 56 (new): The conjugate of claim 53, wherein the high molecular weight polyethylene oxide group is attached to the core or one of said arms.

Claim 57 (new): A plurality of the conjugates of claim 17, wherein the valency platform molecules have a polydispersity of less than about 1.2.

Claim 58 (new): The conjugate of claim 17, wherein the valency platform molecule comprises at least three reactive conjugating groups selected from the group consisting of

hydroxyl, thiol, isocyanate, isothiocyanate, amine, alkyl halide, alkylmercurial halide, aldehyde, ketone, carboxylic acid halide,  $\alpha$ -halocarbonyl,  $\alpha,\beta$ -unsaturated carbonyl, haloformate ester, carboxylic acid, carboxylic ester, carboxylic anhydride, O-acyl isourea, hydrazide, maleimide, imidate ester, sulfonate ester, sulfonyl halide,  $\alpha,\beta$ -unsaturated sulfone, aminooxy, semicarbazide, and  $\beta$ -aminothiol.

Claim 59 (new): The conjugate of claim 17, wherein the valency platform molecule comprises at least 3 aminooxy groups.

Claim 60 (new): The conjugate of claim 17, wherein the valency platform molecule comprises at least 3 carbamate groups.

a<sup>1</sup>  
Claim 61 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the chemically defined valency platform molecule comprises a first and a second polyethylene oxide group, each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 62 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 20,000 Da.

Claim 63 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 22,000 Da.

Claim 64 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 30,000 Da.

Claim 65 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 40,000 Da.

a! Claim 66 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 35,200 Da.

Claim 67 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 39,600 Da.

Claim 68 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 44,000 Da.



Claim 69 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is 22,900-26,400 Da.

Claim 70 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is 24,200-30,800 Da.

Claim 71 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is 26,400-44,000 Da.

a! Claim 72 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is 26,400-39,600 Da.

Claim 73 (new): The conjugate of claim 61, wherein the molecular weight of all polyethylene oxide groups in the valency platform molecule in combination is 26,400-35,200 Da.

Claim 74 (new): The conjugate of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of greater than about 10,000 Da.

Claim 75 (new): The conjugate of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 5,000-10,000 Da.

Claim 76 (new): The conjugate of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 8,000-20,000 Da.

Claim 77 (new): The conjugate of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 10,000-20,000 Da.

Claim 78 (new): The conjugate of claim 61, wherein the chemically defined valency platform molecule comprises a third and a fourth polyethylene oxide group.

a! Claim 79 (new): The conjugate of claim 78, wherein the first, second, third, and fourth polyethylene oxide groups each have a molecular weight of about 8,000-20,000 Da.

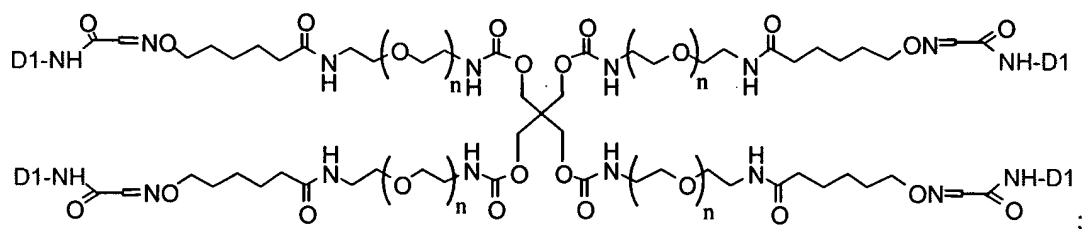
Claim 80 (new): The conjugate of claim 78, wherein the molecular weight of the first, second, third, and fourth polyethylene oxide groups in combination is 26,400-44,000 Da.

Claim 81 (new): The conjugate of claim 61, wherein the biologically active molecule is a  $\beta_2$ GPI domain I polypeptide or analog thereof that specifically binds to a  $\beta_2$ GPI-dependent antiphospholipid antibody.

Claim 82 (new): The conjugate of claim 81, wherein the biologically active molecule is a  $\beta_2$ GPI domain I polypeptide.

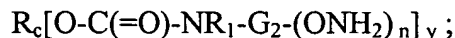
Claim 83 (new): The conjugate of claim 80, wherein the biologically active molecule is a  $\beta_2$ GPI domain I polypeptide.

Claim 84 (new): The conjugate of claim 61, wherein the conjugate has the formula:



wherein the molecular weight of the first, second, third, and fourth polyethylene oxide groups in combination is 26,400-44,000 Da.

a<sup>1</sup>  
Claim 85 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the formula:



wherein y is 2 to 16;

n is 1 to 32;

$R_1$  is H;

$R_c$  is a hydrocarbyl group having from 1 to 200 carbon atoms;

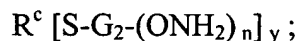
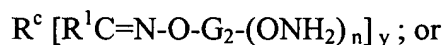
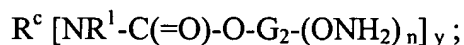
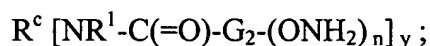
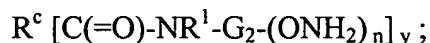
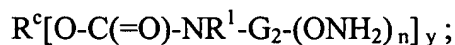
each  $G_2$  independently comprises a polyethylene oxide group having a molecular weight of 44 to 22,000 Da;

wherein each  $G_2$  further comprises an amide group;

with the proviso that the formula comprises at least a first and a second  $G_2$  group, wherein the molecular weight of the polyethylene oxide groups in the first and the second  $G_2$  groups are greater than about 5,000 Da; and

wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 86 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:



wherein:

y is 1 to 16;

n is 1 to 32;

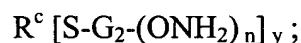
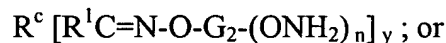
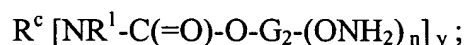
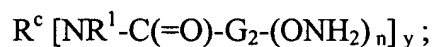
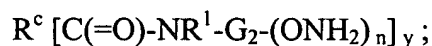
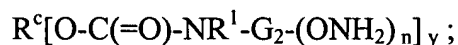
$R^1$  is H, alkyl, heteroalkyl, aryl, heteroaryl or  $G_2-(ONH_2)_n$ ;

$R^c$  is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups; and

$G_2$  is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups;

with the proviso that at least one of the  $R^c$  or  $G_2$  groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.

a<sup>1</sup>  
Claim 87 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:



wherein:

y is 1 to 16;

n is 1 to 32;

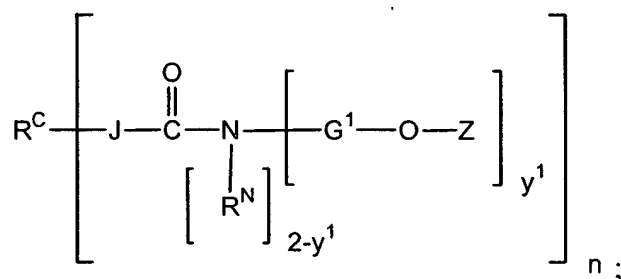
$R^1$  is H, alkyl, heteroalkyl, aryl, heteroaryl or  $G_2-(ONH_2)_n$  ;

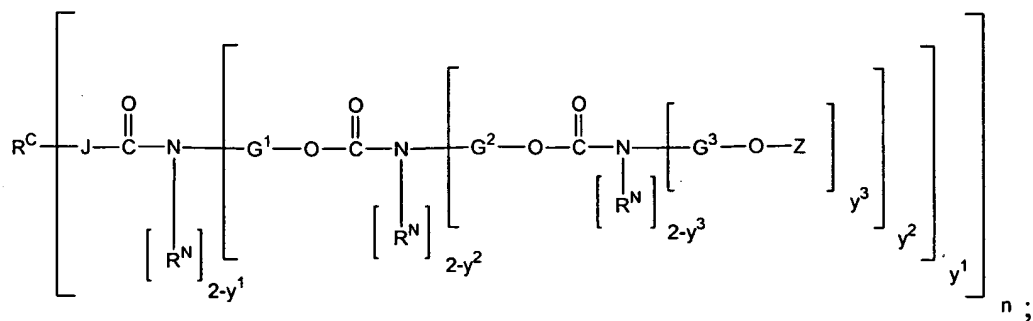
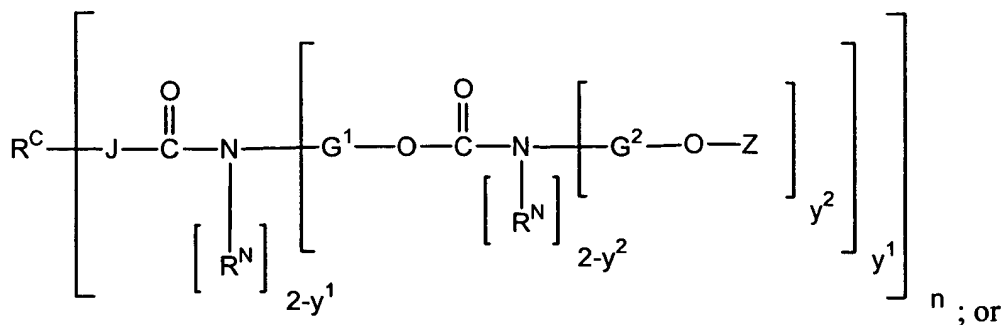
$R^c$  is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups; and

$G_2$  is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

a<sup>1</sup>  
 Claim 88 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

$y^1$ ,  $y^2$ , and  $y^3$  are independently 1 or 2;

J independently denotes either an oxygen atom or a covalent bond;

$R^C$  is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms,

and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms; and

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein  $R^c$  optionally further comprises one or more polyethylene oxide groups;

each  $G^1$ ,  $G^2$ , and  $G^3$  is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each  $G^1$ ,  $G^2$ , and  $G^3$  may independently further comprise one or more polyethylene oxide groups;

each  $R^N$  is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each  $Z$  is independently selected from the group consisting of:

-H

$-C(=O)OR^{CARB}$

$-C(=O)R^{ESTER}$

$-C(=O)NR^A R^B$

$-C(=O)NR^{AB}$



wherein:

each  $R^{\text{CARB}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

each  $R^{\text{ESTER}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

each monovalent  $R^{\text{A}}$  and  $R^{\text{B}}$  is independently H or an organic group comprising from 1 to 20 carbon atoms;

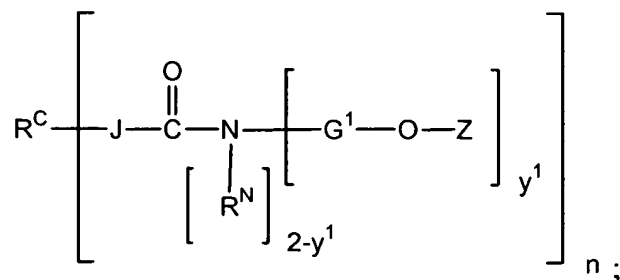
each divalent  $R^{\text{AB}}$  is independently an organic group comprising from 1 to 20 carbon atoms; and

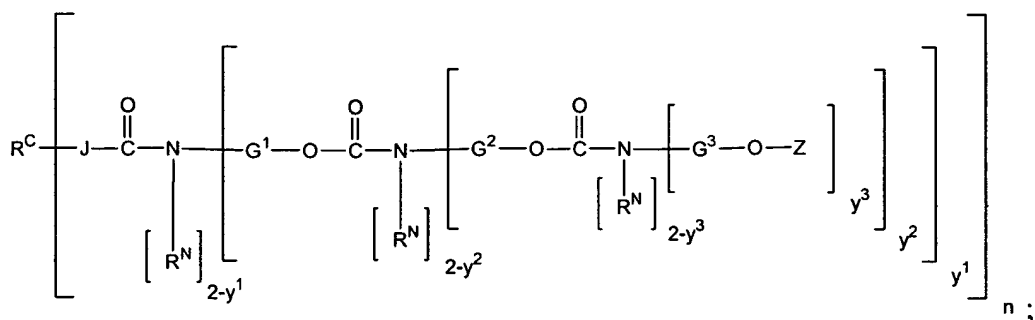
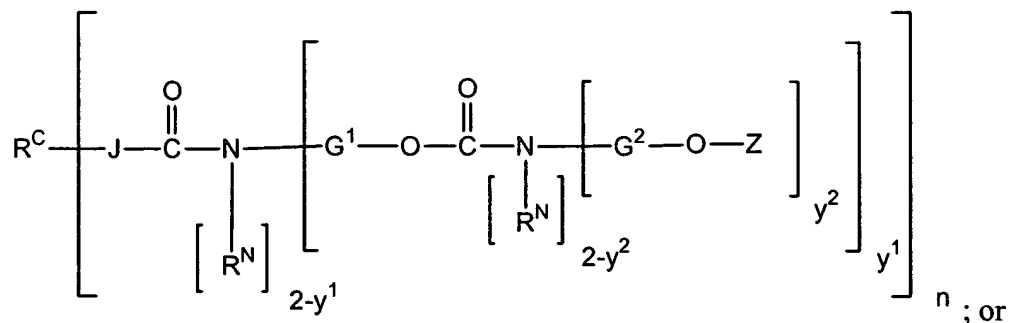
wherein, when Z is  $-\text{C}(=\text{O})\text{OR}^{\text{CARB}}$ ,  $-\text{C}(=\text{O})\text{R}^{\text{ESTER}}$ ,  $-\text{C}(=\text{O})\text{NR}^{\text{A}}\text{R}^{\text{B}}$ , or  $-\text{C}(=\text{O})\text{NR}^{\text{AB}}$ , Z further comprises a reactive conjugating functional group;

with the proviso that at least one of the  $R^{\text{c}}$ ,  $G^1$ ,  $G^2$ , or  $G^3$  groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.

a

Claim 89 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

$y^1$ ,  $y^2$ , and  $y^3$  are independently 1 or 2;

J independently denotes either an oxygen atom or a covalent bond;

$R^C$  is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms,

and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms; and

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R<sup>c</sup> optionally further comprises one or more polyethylene oxide groups;

each G<sup>1</sup>, G<sup>2</sup>, and G<sup>3</sup> is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G<sup>1</sup>, G<sup>2</sup>, and G<sup>3</sup> may independently further comprise one or more polyethylene oxide groups;

each R<sup>N</sup> is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR<sup>CARB</sup>

-C(=O)R<sup>ESTER</sup>

-C(=O)NR<sup>A</sup>R<sup>B</sup>

-C(=O)NR<sup>AB</sup>

wherein:

each  $R^{\text{CARB}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

each  $R^{\text{ESTER}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

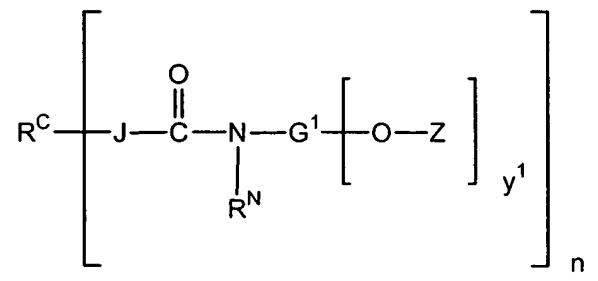
each monovalent  $R^A$  and  $R^B$  is independently H or an organic group comprising from 1 to 20 carbon atoms;

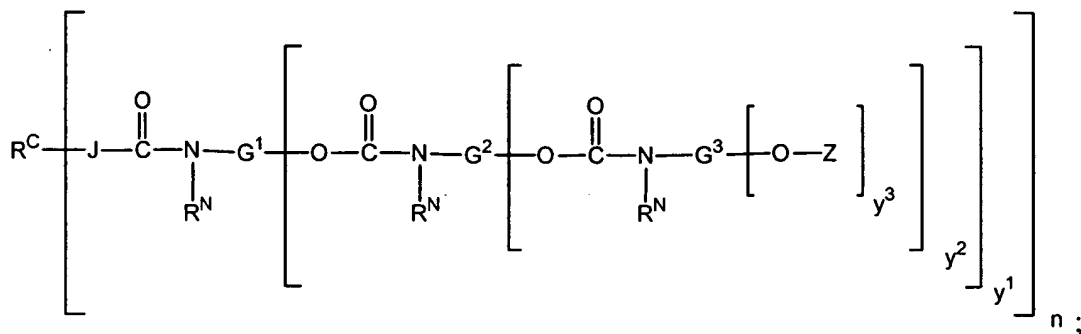
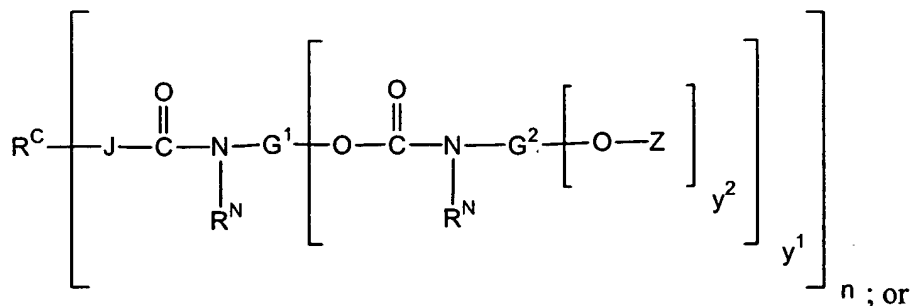
each divalent  $R^{\text{AB}}$  is independently an organic group comprising from 1 to 20 carbon atoms; and

wherein, when Z is  $-\text{C}(=\text{O})\text{OR}^{\text{CARB}}$ ,  $-\text{C}(=\text{O})\text{R}^{\text{ESTER}}$ ,  $-\text{C}(=\text{O})\text{NR}^A\text{R}^B$ , or  $-\text{C}(=\text{O})\text{NR}^{\text{AB}}$ , Z further comprises a reactive conjugating functional group;

a<sup>1</sup>  
with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 90 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

y<sup>1</sup>, y<sup>2</sup>, and y<sup>3</sup> are independently a positive integer from 1 to 10;

J independently denotes either an oxygen atom or a covalent bond;

R<sup>C</sup> is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms,

and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein  $R^c$  optionally further comprises one or more polyethylene oxide group;

each  $G^1$ ,  $G^2$ , and  $G^3$  is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms,

and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each  $G^1$ ,  $G^2$ , and  $G^3$  may independently further comprise one or more polyethylene oxide groups;

each  $R^N$  is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each  $Z$  is independently selected from the group consisting of:

-H

$-C(=O)OR^{CARB}$

$-C(=O)R^{ESTER}$

$-C(=O)NR^A R^B$

$-C(=O)NR^{AB}$

wherein:

each  $R^{\text{CARB}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

each  $R^{\text{ESTER}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

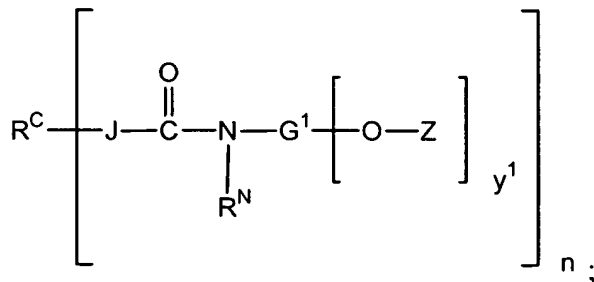
each monovalent  $R^A$  and  $R^B$  is independently H or an organic group comprising from 1 to 20 carbon atoms;

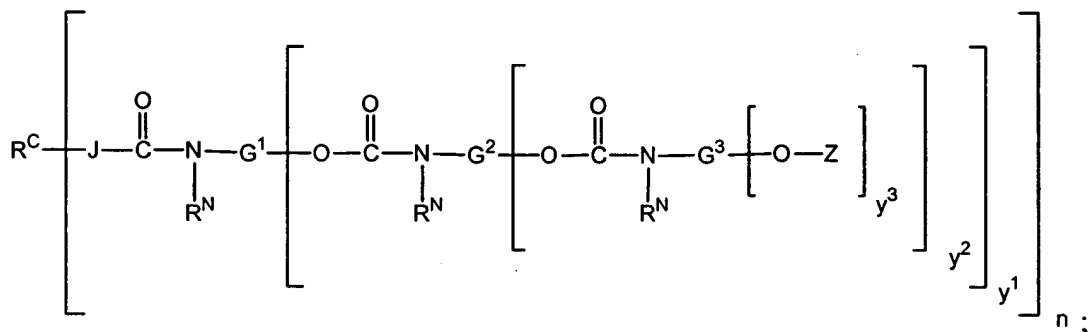
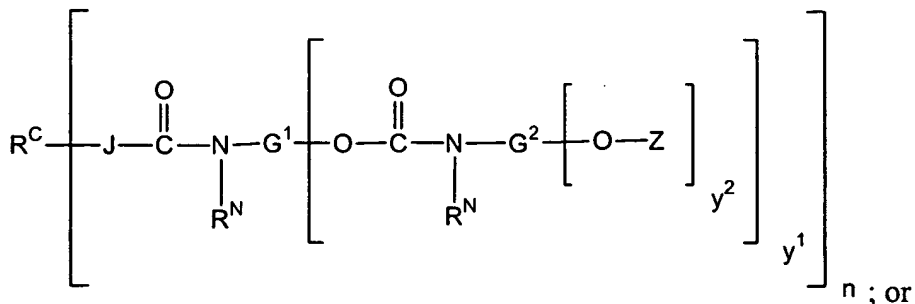
each divalent  $R^{\text{AB}}$  is independently an organic group comprising from 1 to 20 carbon atoms; and

wherein, when Z is  $-\text{C}(=\text{O})\text{OR}^{\text{CARB}}$ ,  $-\text{C}(=\text{O})\text{R}^{\text{ESTER}}$ ,  $-\text{C}(=\text{O})\text{NR}^A\text{R}^B$ , or  $-\text{C}(=\text{O})\text{NR}^{\text{AB}}$ , Z further comprises a reactive conjugating functional group;

with the proviso that at least one of the  $R^c$ ,  $G^1$ ,  $G^2$ , or  $G^3$  groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.

Claim 91 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

$y^1$ ,  $y^2$ , and  $y^3$  are independently a positive integer from 1 to 10;

J independently denotes either an oxygen atom or a covalent bond;

$R^C$  is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms,

and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;



and wherein  $R^c$  optionally further comprises one or more polyethylene oxide groups;

each  $G^1$ ,  $G^2$ , and  $G^3$  is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each  $G^1$ ,  $G^2$ , and  $G^3$  may independently further comprise one or more polyethylene oxide groups;

each  $R^N$  is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each  $Z$  is independently selected from the group consisting of:

-H

$-C(=O)OR^{CARB}$

$-C(=O)R^{ESTER}$

$-C(=O)NR^A R^B$

$-C(=O)NR^{AB}$

wherein:

each  $R^{\text{CARB}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

each  $R^{\text{ESTER}}$  is independently an organic group comprising from 1 to about 20 carbon atoms;

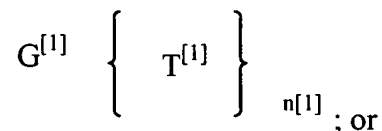
each monovalent  $R^{\text{A}}$  and  $R^{\text{B}}$  is independently H or an organic group comprising from 1 to 20 carbon atoms;

each divalent  $R^{\text{AB}}$  is independently an organic group comprising from 1 to 20 carbon atoms; and

wherein, when Z is  $-\text{C}(=\text{O})\text{OR}^{\text{CARB}}$ ,  $-\text{C}(=\text{O})\text{R}^{\text{ESTER}}$ ,  $-\text{C}(=\text{O})\text{NR}^{\text{A}}\text{R}^{\text{B}}$ , or  $-\text{C}(=\text{O})\text{NR}^{\text{AB}}$ , Z further comprises a reactive conjugating functional group;

a  
with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 92 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:



$$G^{[2]} \left\{ L^{[2]} - J^{[2]} - Z^{[2]} (T^{[2]})_{p[2]} \right\}_{n[2]};$$

wherein

each of  $G^{[1]}$  and  $G^{[2]}$ , if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein  $G^{[1]}$  and  $G^{[2]}$ , if present, optionally further comprises one or more polyethylene oxide groups;

each  $T^{[1]}$  and each  $T^{[2]}$ , if present, is independently chosen from the group  $NHR^{SUB}$ ,  $C(=O)NHNHR^{SUB}$ ,  $NHNHR^{SUB}$ ,  $C(=O)OH$ ,  $C(=O)OR^{ESTER}$ ,  $C(=O)OC(=O)R^B$ ,  $C(=O)X$ ,  $S(=O)_2X$ ,  $C(=NR^{SUB})OR^{SUB}$ ,  $NCO$ ,  $NCS$ ,  $OC(=O)X$ ,  $C(=O)OC(=NR^{SUB})NHR^{SUB}$ ,  $C(=O)H$ ,  $C(=O)R^B$ ,  $SH$ ,  $OH$ ,  $C(=O)CH_2X$ ,  $R^{ALK}X$ ,  $S(=O)_2OR^{ALK}X$ ,  $N-C(=O)CH=CHC(=O)-$ ,  $C(=O)CR^B=CR^B_2$ ,  $R^{ALK}-Hg-X$ ,  $S(=O)CR^B=CR^B_2$ , and  $ONH_2$ ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each  $R^{ALK}$  is independently a linear, branched, or cyclic alkyl (1-20C) group;

each  $R^{SUB}$  is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each  $R^{ESTER}$  is independently N-succinimidyl, p-nitrophenyl, pentafluorophenyl, tetrafluorophenyl, pentachlorophenyl, 2,4,5-trichlorophenyl, 2,4-dinitrophenyl, cyanomethyl, 5-chloro, 8-quinolone, 1-piperidine, or N-benzotriazole;

each  $R^B$  is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;  
 each  $L^{[2]}$ , if present, is independently chosen from the group O,  $NR^{SUB}$  and S;  
 each  $J^{[2]}$ , if present, is independently chosen from the group  $C(=O)$  and  $C(=S)$ ;  
 each  $Z^{[2]}$ , if present, is independently a radical comprising 1-200 atoms selected from the group C, H, N, O, Si, P and S, and forming attachment sites for at least  $p^{[2]}$  functional groups, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein  $Z^{[2]}$ , if present, optionally further comprises one or more polyethylene oxide groups;

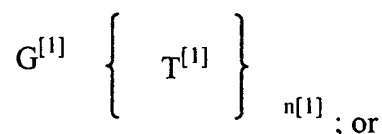
$n^{[1]}$ , if present, is 1 to 32;

$n^{[2]}$ , if present, is 1 to 32; and

$p^{[2]}$ , if present, is 1 to 8; with the proviso that the product  $n^{[2]} \times p^{[2]}$  be greater than 1 and less than 33;

with the proviso that at least one of the  $G^{[1]}$ ,  $G^{[2]}$ , or  $Z^{[2]}$  groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.

Claim 93 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:



$$G^{[2]} \left\{ L^{[2]} - J^{[2]} - Z^{[2]} (T^{[2]})_{p[2]} \right\}_{n[2]};$$

wherein

each of  $G^{[1]}$  and  $G^{[2]}$ , if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein  $G^{[1]}$  and  $G^{[2]}$ , if present, optionally further comprises one or more polyethylene oxide groups;

each  $T^{[1]}$  and each  $T^{[2]}$ , if present, is independently chosen from the group  $NHR^{SUB}$ ,  $C(=O)NHNHR^{SUB}$ ,  $NHNHR^{SUB}$ ,  $C(=O)OH$ ,  $C(=O)OR^{ESTER}$ ,  $C(=O)OC(=O)R^B$ ,  $C(=O)X$ ,  $S(=O)_2X$ ,  $C(=NR^{SUB})OR^{SUB}$ ,  $NCO$ ,  $NCS$ ,  $OC(=O)X$ ,  $C(=O)OC(=NR^{SUB})NHR^{SUB}$ ,  $C(=O)H$ ,  $C(=O)R^B$ ,  $SH$ ,  $OH$ ,  $C(=O)CH_2X$ ,  $R^{ALK}X$ ,  $S(=O)_2OR^{ALK}X$ ,  $N-C(=O)CH=CHC(=O)-$ ,  $C(=O)CR^B=CR^B_2$ ,  $R^{ALK}-Hg-X$ ,  $S(=O)CR^B=CR^B_2$ , and  $ONH_2$ ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each  $R^{ALK}$  is independently a linear, branched, or cyclic alkyl (1-20C) group;

each  $R^{SUB}$  is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each  $R^{ESTER}$  is independently N-succinimidyl, p-nitrophenyl, pentafluorophenyl, tetrafluorophenyl, pentachlorophenyl, 2,4,5-trichlorophenyl, 2,4-dinitrophenyl, cyanomethyl, 5-chloro, 8-quinolone, 1-piperidine, or N-benzotriazole;

each  $R^B$  is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;  
each  $L^{[2]}$ , if present, is independently chosen from the group O,  $NR^{SUB}$  and S;  
each  $J^{[2]}$ , if present, is independently chosen from the group  $C(=O)$  and  $C(=S)$ ;  
each  $Z^{[2]}$ , if present, is independently a radical comprising 1-200 atoms selected from the group C, H, N, O, Si, P and S, and forming attachment sites for at least  $p^{[2]}$  functional groups, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein  $Z^{[2]}$ , if present, optionally further comprises one or more polyethylene oxide groups;

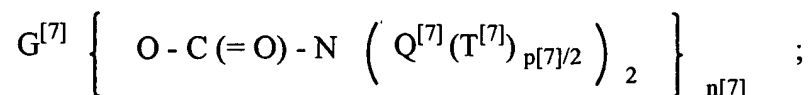
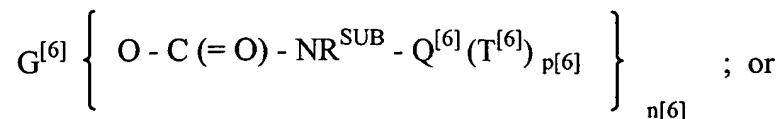
$n^{[1]}$ , if present, is 1 to 32;

$n^{[2]}$ , if present, is 1 to 32;

$p^{[2]}$ , if present, is 1 to 8; with the proviso that the product  $n^{[2]} \times p^{[2]}$  be greater than 1 and less than 33;

a<sup>1</sup>  
with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 94 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:



wherein

each of  $G^{[6]}$  and  $G^{[7]}$ , if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein  $G^{[6]}$  and  $G^{[7]}$ , if present, optionally further comprises one or more polyethylene oxide groups;

each  $T^{[6]}$  and each  $T^{[7]}$ , if present, is independently chosen from the group  $NHR^{SUB}$ ,  $C(=O)NHNHR^{SUB}$ ,  $NHNHR^{SUB}$ ,  $C(=O)OH$ ,  $C(=O)OR^{ESTER}$ ,  $C(=O)OC(=O)R^B$ ,  $C(=O)X$ ,  $S(=O)_2X$ ,  $C(=NR^{SUB})OR^{SUB}$ ,  $NCO$ ,  $NCS$ ,  $OC(=O)X$ ,  $C(=O)OC(=NR^{SUB})NHR^{SUB}$ ,  $C(=O)H$ ,  $C(=O)R^B$ ,  $SH$ ,  $OH$ ,  $C(=O)CH_2X$ ,  $R^{ALK}X$ ,  $S(=O)_2OR^{ALK}X$ ,  $N-C(=O)CHCHC(=O)-$ ,  $C(=O)CR^B=CR^B_2$ ,  $R^{ALK}-Hg-X$ ,  $S(=O)CR^B=CR^B_2$ , and  $ONH_2$ ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each  $R^{ALK}$  is independently a linear, branched, or cyclic alkyl (1-20C) group;

each  $R^{SUB}$  is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

each  $R^{\text{ESTER}}$  is independently N-hydroxysuccinimidyl, p-nitrophenoxy, or pentafluorophenoxy;

each  $R^B$  is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

$n^{[6]}$ , if present, is 1 to 32;

$p^{[6]}$ , if present, is 1 to 8;

with the proviso that the product  $n^{[6]} \times p^{[6]}$  be greater than 1 and less than 33;

$n^{[7]}$ , if present, is 1 to 32;

$p^{[7]}$ , if present, is 1 to 8;

with the proviso that the product  $n^{[7]} \times p^{[7]}$  be greater than 1 and less than 33;

each  $Q^{[6]}$  and each  $Q^{[7]}$ , if present, is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, and wherein each  $Q^{[6]}$  and  $Q^{[7]}$  moiety, if present, forms attachment sites for at least  $p^{[6]}$  or  $p^{[7]/2}$  functional groups, respectively, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

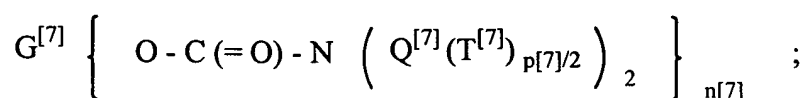
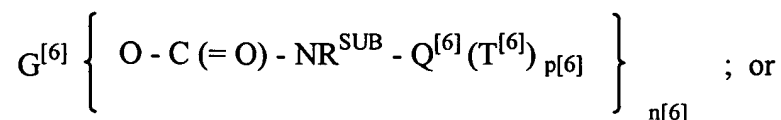
and wherein  $Q^{[6]}$  and  $Q^{[7]}$ , if present, optionally further comprises one or more polyethylene oxide groups; and

wherein  $p^{[7]/2}$  is an integer;

with the proviso that at least one of the  $G^{[6]}$ ,  $G^{[7]}$ ,  $Q^{[6]}$ , or  $Q^{[7]}$  groups comprises a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.



Claim 95 (new): A conjugate of a chemically defined valency platform molecule and a biologically active molecule, wherein the valency platform molecule prior to conjugation with the biologically active molecule has the structure of one of the following formulae:



wherein

each of  $G^{[6]}$  and  $G^{[7]}$ , if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein  $G^{[6]}$  and  $G^{[7]}$ , if present, optionally further comprises one or more polyethylene oxide groups;

each  $T^{[6]}$  and each  $T^{[7]}$ , if present, is independently chosen from the group  $NHR^{SUB}$ ,  $C(=O)NHNHR^{SUB}$ ,  $NHNHR^{SUB}$ ,  $C(=O)OH$ ,  $C(=O)OR^{ESTER}$ ,  $C(=O)OC(=O)R^B$ ,  $C(=O)X$ ,  $S(=O)_2X$ ,  $C(=NR^{SUB})OR^{SUB}$ ,  $NCO$ ,  $NCS$ ,  $OC(=O)X$ ,  $C(=O)OC(=NR^{SUB})NHR^{SUB}$ ,  $C(=O)H$ ,  $C(=O)R^B$ ,  $SH$ ,  $OH$ ,  $C(=O)CH_2X$ ,  $R^{ALK}X$ ,  $S(=O)_2OR^{ALK}X$ ,  $N-C(=O)CHCHC(=O)-$ ,  $C(=O)CR^B=CR^B_2$ ,  $R^{ALK}-Hg-X$ ,  $S(=O)CR^B=CR^B_2$ , and  $ONH_2$ ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each  $R^{ALK}$  is independently a linear, branched, or cyclic alkyl (1-20C) group;

each  $R^{SUB}$  is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

each  $R^{ESTER}$  is independently N-hydroxysuccinimidyl, p-nitrophenoxy, or pentafluorophenoxy;

each  $R^B$  is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

$n^{[6]}$ , if present, is 1 to 32;

$p^{[6]}$ , if present, is 1 to 8;

with the proviso that the product  $n^{[6]} \times p^{[6]}$  be greater than 1 and less than 33;

$n^{[7]}$ , if present, is 1 to 32;

$p^{[7]}$ , if present, is 1 to 8;

with the proviso that the product  $n^{[7]} \times p^{[7]}$  be greater than 1 and less than 33;

a<sup>1</sup>  
each  $Q^{[6]}$  and each  $Q^{[7]}$ , if present, is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, , and wherein each  $Q^{[6]}$  and  $Q^{[7]}$  moiety, if present, forms attachment sites for at least  $p^{[6]}$  or  $p^{[7]/2}$  functional groups, respectively, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein  $Q^{[6]}$  and  $Q^{[7]}$ , if present, optionally further comprises one or more polyethylene oxide groups; and

wherein  $p^{[7]/2}$  is an integer;

with the proviso that the valency platform molecule comprises at least 2

polyethylene oxide groups each having a molecular weight of greater than about 5,000

a' Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

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